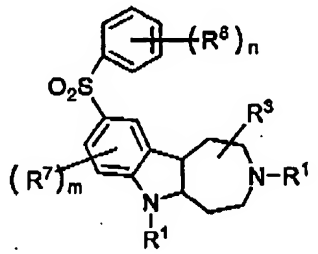
Amendments to the Specification:

Please replace the "paragraph" in the Specification starting on page 3, line 22 continuing until page 5, line 15, with the following:

The present invention provides a compound of formula I



I

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof,

wherein each R^1 is independently

a) H,

b) C_{1-4} alkyl,

c) C_{1-4} alkyl substituted by a phenyl where the phenyl is optionally substituted with one or two R^2, or

d) phenyl, optionally substituted with one or two R^2;

R^2 is

a) halo,

b) OR^3,

c) CF_3

d) $C(=O)-NR^4R^5$,

e) $NH-SO_2-R^6$,

f) NR^4R^5,

g) $NR^4-C(=O)-R^4$,

h) $SO_2-NR^4R^5$,

i) CN, or

j) NO_2;

R^3 is H, C_{1-4} alkyl, or phenyl;

R^4 and R^5 are independently H, C_{1-4} alkyl, or R^4 and R^5 taken together with the attached nitrogen atom to form a ring selected from the group consisting of 1-pyrrolidinyl, 1-piperazinyl and 1-morpholinyl;

R^6 is H or C_{1-4} alkyl;

R^7 is

a) H, or
b) halo,
c) OR^3,
d) CF_3
e) $C(=O)-NR^4R^5$,
f) $NH-SO_2-R^6$,
g) NR^4R^5,
h) $NR^4-C(=O)-R^4$,
i) $SO_2-NR^4R^5$,
j) CN, or
k) NO_2;

R^8 is

a) H,
b) F,
c) Cl,
d) C_{1-4} alkyl,
e) C_{1-3} alkoxy,
f) CF_3,
g) C_{1-4} alkyl substituted by a phenyl wherein the phenyl is optionally substituted with one or two R^2,
h) phenyl, optionally substituted with one or two R^2,
i) OR^3,
j) $CO-NR^4R^5$,
k) NR^4R^5,

l) $NH\text{-}SO_2\text{-}R^6$, or

m) $NH\text{-}CO\text{-}R^4$;

at each occurrence, alkyl and alkoxy is optionally substituted with OH, halo, or NH_2;

m is 1 to 2; and n is 1-3.

On page 8, lines 12-23: Please replace the paragraph at said location with:

Prodrugs of the compounds of Formula I are an embodiment of the present invention. The term "prodrug" refers to compounds that are rapidly transformed in vivo to yield the parent compound of the above formula, for example, by hydrolysis in blood. Prodrugs are discussed in T. Higuchi and V. Stella, "Pro-drugs as Novel Delivery Systems," Vol. 14 of the A.C.S. Symposium Series; in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987; in Notari, R. E., "Theory and Practice of Prodrug Kinetics," Methods in Enzymology, 112:309-323 (1985); in Bodor, N., "Novel Approaches in Prodrug Design," Drugs of the Future, 6(3):165-182 (1981); and in Bundgaard, H., "Design of Prodrugs: Bioreversible-Derivatives for Various Functional Groups and Chemical Entities," in Design of Prodrugs (H. Bundgaard, ed.), Elsevier, N.Y. (1985) ~~all of which are incorporated herein by reference~~.

On page 34,line 5 to page 35, line 7, please replace the paragraph at said location with the following:

In Scheme I, the starting material 1 can be prepared according to the procedures described in US patent application, Serial No. 09/613843, now US6,468,999 B1 entitled as 1,2,3,4,5,6-hexahydroazepino[4,5-b]indoles containing arylsulfones at the 9-position.

The unsubstituted 9-arylsulfones (IX) and substituted 9-arylsulfones (X) are both prepared by means known to those skilled in the art. The term 9-arylsulfones (XII) includes both the unsubstituted 9-arylsulfones (IX), where R_3 is -H and substituted 9-arylsulfones (X) where R_3 is $\neq$ to –H. The process of preparation can be viewed as being in two parts. The first part is the production of the appropriately substituted hydrazone (V), see CHART A. The second part is the coupling and reaction of the appropriately substituted hydrazone (V) with the 1-protected hexahydro-4H-azepine-4-one (VI) to give the intermediate (VII) and its transformation to the unsubstituted 9-arylsulfone (IX), see CHART B.

The appropriately substituted thiols (I) are either known to those skilled in the art or can be readily prepared from known starting materials by means well known to those skilled in the art. There can be either one or two R_9 substituents and R_9 includes –H, -F, -Cl, C_1-C_3 alkyl, C_1-C_3 alkoxy and $-CF_3$; it is preferred that R_9 is –H, -F, -Cl, C_1 alkyl, C_1 alkoxy, and
$-CF_3$ and when F- it is preferred that it be in the 4- or *p*-position. It is preferred that the R_9 substituent be in either the 3- or 4-position.

The appropriately substituted thiol (I) is coupled with the appropriately substituted 4-chloro-1-nitrobenzene (II) by known means to produce the thioether (III). There can be either one or two R_x groups. If R_x is other than -H, it should be part of the 4-chloro-1-nitrobenzene (II) so that it will become part of the final unsubstituted 9-arylsulfone (IX) when it is formed. It is most difficult to add the R_x substitutent (other than -H) to the unsubstituted 9-arylsulfone (IX) once it is formed. Therefore, the R_x group should be part of the appropriately substituted 4-chloro-1-nitrobenzene (II) when it is reacted with the thiol (I). R_x includes of –H, -F and -Cl; it is preferred that R_x is -H. The thioether (III) is then oxidized with hydrogen peroxide (30%) followed by reduction with rhodium on carbon (5%), all of which is known to those skilled in the art, to produce the amine (IV). The amine (IV) is then diazotized by (sodium) nitrite and (hydrochloric) acid followed by reduction with tin chloride/water to give the corresponding hydrazine (V).

The second part of the reaction, is well known to those skilled in the art, see US Patents 3,652,588, 3,676,558 and 3,839,357. The only difference between the process in those patents and that here is the arylsulfone substituent at the 9-position. That substituent is already in place in the hydrazine (V) prior to the reaction of the 9-arylsulfone hydrazine (V) with the 1-protected hexahydro-4H-azepine-4-one (VI) to produce the correspondingly substituted intermediate (VII). Suitable protecting groups (PG) include ϕ-CH_2-, ϕ-CO-, ϕ-CH_2-CO_2- and -CO-O-$C(CH_3)_3$; it is preferred that the protecting group be ϕ-CH_2- or ϕ-CO-. The cyclization of the intermediate (VII) to the corresponding protected arylsulfone (VIII) and then the deprotection to the unsubstituted 9-arylsulfone (IX) all follow known methods. The protecting groups (PG) are readily removed by means well known to those skilled in the art. The unsubstituted 9-arylsulfone (IX) can then be substituted at the C3-position (R_3, ring nitrogen atom) as well as on the indole nitrogen (R_N) as is known to those

skilled in the art. Alternatively, arylsulfone (VIII) can be alkylated with the desired R_N-X substituent to give the protected indole (XI) which then is deprotected to give the desired substituted 9-arylsulfone (X). Useful R_3 groups include of –H and C_1-C_2 alkyl; it is preferred that R_3 be -H. Useful R_N groups include of –H and C_1-C_4 alkyl; it is preferred that R_N is -H, C_1 alkyl and C_2 alkyl. The invention here is not the process chemistry but rather the novel products produced. -ϕ refers to phenyl (C_6H_5).

The preferred protecting group for the intermediates (VI), (VII) and (VIII) are benzyl and benzamide though other groups are operable as is known to those skilled in the art.

The 9-arylsulfones (XI) are amines, and as such form acid addition salts when reacted with acids of sufficient strength. Pharmaceutically acceptable salts include salts of both inorganic and organic acids. The pharmaceutically acceptable salts are preferred over the corresponding free amines since they produce compounds which are more water soluble and more crystalline. The preferred pharmaceutically acceptable salts include salts of the following acids methanesulfonic, hydrochloric, hydrobromic, sulfuric, phosphoric, nitric, benzoic, citric, tartaric, fumaric, maleic, CH_3-$(CH_2)_n$-COOH where n is 0 thru 4, HOOC-$(CH_2)_N$-COOH where n is as defined above.

CHART A

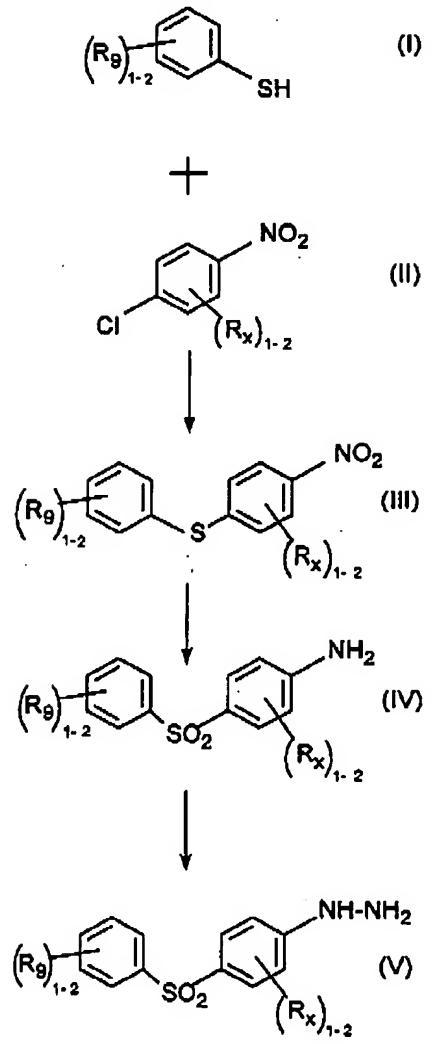


CHART B

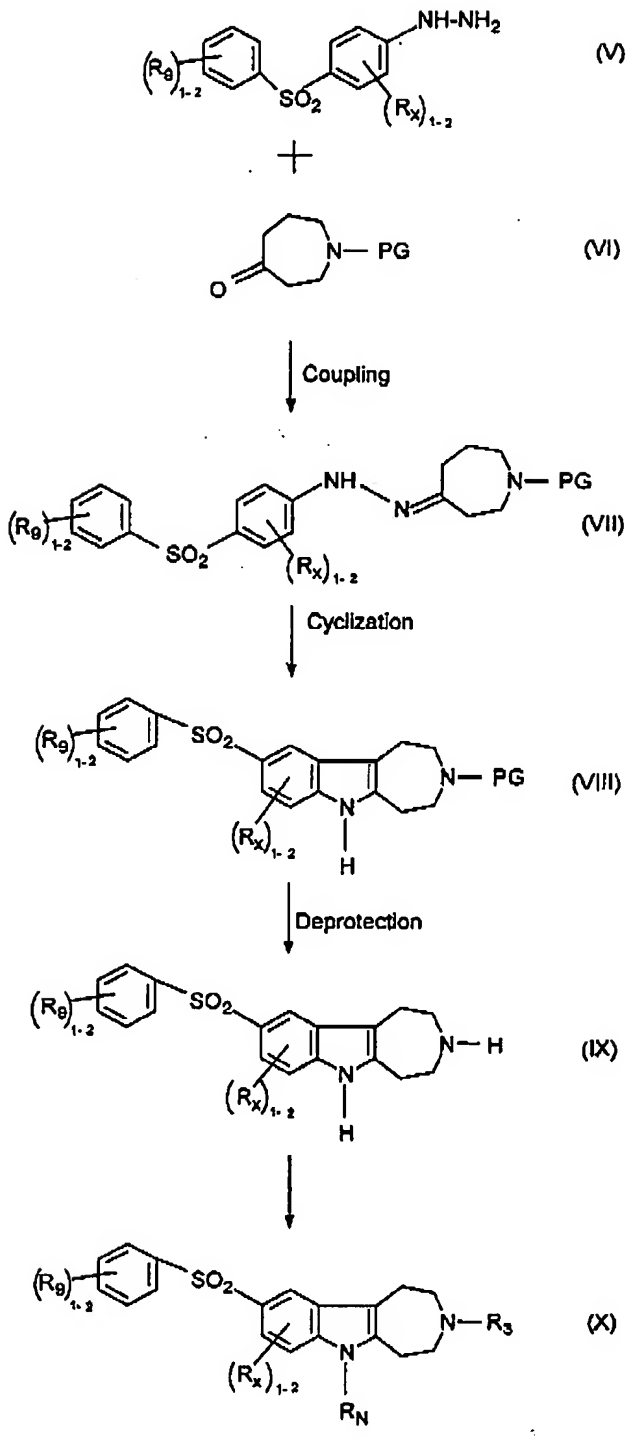
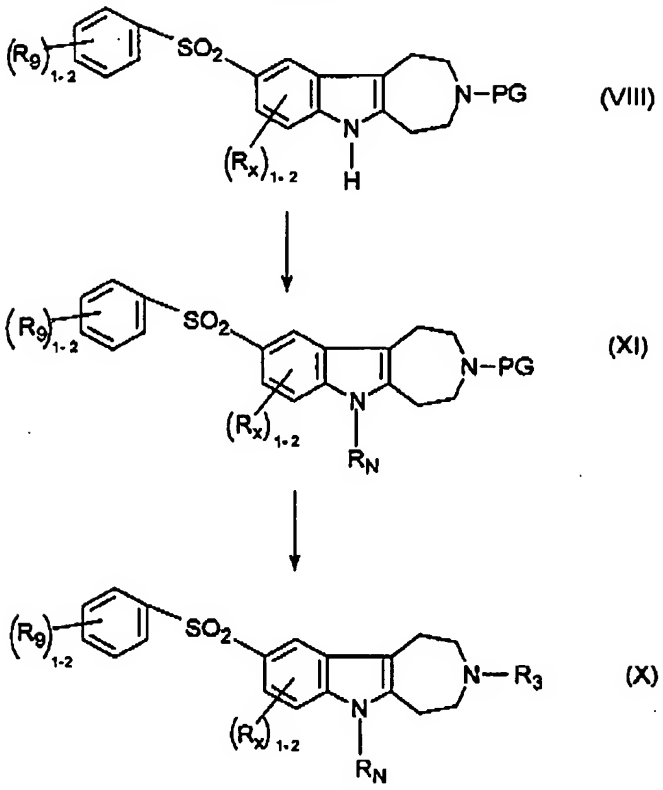

NH-NH2
(V)
SO2
(Rx)1-2
(Rg)1-2
N— PG
(VI)
O
Coupling
NH
N
(VII)
Cyclization
(VIII)
H
Deprotection
N— H
(IX)
N— R3
(X)
RN

CHART C



The *cis*- and *trans*-indolines can be prepared stereoselectively. To prepare *cis*-indolines 4 and 5 the following method is used. Treatment of compound 1 with a reducing agent such as sodium cyanoborohydride in the presence of trifluoroacetic acid (TFA) in a solvent such as methanol at 0 °C provides reduced *cis*-indoline 2. Protection of this crude mixture as the *tert*-butyl carbamate (3) can be carried out as using di-*tert*-butyl dicarbonate in a solvent such as CH_2Cl_2 at ambient temperature. The enantiomers can be separated by chiral (Chiracel OD-H) HPLC to give the individual *cis*-enantiomers 4 and 5. Deprotection using TFA/CH_2Cl_2 or HCl/MeOH provides the individual enantiomers 8 and 9, respectively. Compounds 8 or 9 can be further alkylated by the procedures well known to one skilled in the art.